UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/067,104	02/04/2002	Jeffery A. Bluestone	TOLT:006USD4	5806

7590 07/15/2004

Gina N. Shishima
FULBRIGHT & JAWORSKI L.L.P.
Suite 2400
600 Congress Avenue
Austin, TX 78701

EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/067,104	BLUESTONE, JEFFERY A.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on 3/12/04

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1,8,14-26 and 28 is/are pending in the application.

4a) Of the above claim(s) 14,15,20 and 25 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,8,16-19,21-24,26 and 28 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and the Declaration of Jeffrey A. Bluestone under 37 CFR 1.132 both filed 3/12/04 are acknowledged and have been entered.

2. Applicant is reminded of Applicant's election without traverse of the species OKT3 as the immunopotentiating protein and a tumor-specific or tumor-associated antigen as the second compound having an epitope in Paper No. 6.

Upon consideration of the prior art, the search has been extended to include the species of viral specific or associated epitope, and hepatitis surface antigen and HIV env-associated antigen gp120 T1 or T2.

Accordingly, claims 14, 15, 20 and 25 (non-elected species) remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 1, 8, 16-19, 21-24, 26 and 28 are currently being examined.

3. The disclosure is objected to because of the following informalities:

In the Brief Description of the Drawings: Figure 8 should be Figure 8 A-D, but has been amended by Applicant as Figure 8A-B.

Appropriate corrections are required.

The following are new grounds of rejection necessitated by Applicant's said amendment and said Declaration of Dr. Bluestone both filed 3/12/04.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 7 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 7 recites the limitation "The composition of claim 7". There is insufficient antecedent basis for this limitation in the claims.

b. Claim 26 recites the limitation "the immunopotentiating protein". There is insufficient antecedent basis for this limitation in the claims.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1, 8, 16-19, 21-24, 26 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 4,772,547 (previously provided) in view of Mezzanzanica et al (Int. J. Cancer, 41, 609-615, 1988, previously provided), Anderson et al (J. Immunol. 142(4): 1383-1394, 2/15/1989) and EP 0273716A2 (previously provided).

US Patent No. 4,772,547 discloses vaccine compositions comprising antigenic peptides and proteins from hepatitis surface antigens and HIV envelope and adjuvants such as IFN, IL-2, thymosin alpha 1 (especially column 8 at lines 25-49). US Patent No. 4,772,547 further discloses enhancing immunogenicity of the peptides by coupling the peptides covalently (via Cys, i.e., by "crosslinking") to toxoids or carrier materials that enhance immunogenicity. Claim 26 is included in the instant rejection because the instant specification discloses conjugation being in the nature of a chemical or molecular crosslink (page 15 at lines 25-30).

US Patent No. 4,772,547 does not disclose a heteroconjugate comprising anti-CD3 mAb directed against the non-polymorphic TCR-associated CD3 chains, γ, δ, ε or ζ coupled or fused to a second protein having an epitope against which a cellular or humoral immune response is desired.

Mezzanzanica et al teach anti-CD3 mAb OKT3 and a defined target antigen on human ovarian carcinoma cells and an antibody against the said antigen (especially page 609, column 2, MAbs section). Mezzanzanica et al further teach antibodies comprising anti-CD3 antibodies administered in humans to induce T cells.

Anderson et al teach the activation of T cells and NK cells using anti-CD3 mAb and IL-2 for anti-tumor activity. Anderson et al further teach the anti-human CD3 mAb, OKT3.

EP 0273716 A2 teaches HIV gp120 envelope protein antigen of HIV and T1 and T2 antigenic peptides and treatment of HIV (especially page 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the mAb OKT3 taught by Mezzanzanica et al and Anderson et al in the composition disclosed by US Patent No. 4,772,547 comprising antigenic peptides from viral proteins such as HIV or those HIV antigenic peptides taught by EP 0273716 A2 or comprising tumor antigens such as those taught by Mezzanzanica et al and adjuvants such as IL-2 disclosed by US Patent No. 4,772,547 or as taught by Anderson et al, and in addition, to have cross-linked the OKT3 mAb to the said antigenic peptide(s).

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a composition that could stimulate T cells for anti-tumor or anti-viral immunity because US Patent No. 4,772,547 discloses coupling peptides covalently by cross-linkage to a carrier material to enhance immunogenicity and use with IL-2 in anti-viral vaccine compositions, Anderson et al teach the activation of T cells using anti-CD3 mAb such as OKT3 for activation of anti-tumor T cell immunity, since Mezzanzanica et al teach antibodies comprising anti-CD3 antibodies administered in humans to induce T cells, and since Mezzanzanica et al teach target tumor antigens, US Patent No. 4,772,547 discloses viral peptide antigens for vaccine use, and EP 0273716 A2 teaches the HIV T1 and T2 antigenic peptides and treatment of HIV.

The motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Section MPEP 2144.07.

8. Claims 1, 8, 16-19, 21-24, 26 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 4,772,547 (previously provided) in view of Mezzanzanica et al (Int. J. Cancer, 41, 609-615, 1988, previously provided), Anderson et al (Cancer Immunology and Immunother. 1988 27: 82-88) and EP 0273716A2 (previously provided).

US Patent No. 4,772,547 discloses vaccine compositions comprising antigenic peptides and proteins from hepatitis surface antigens and HIV envelope and adjuvants such as IFN, IL-2, thymosin alpha 1 (especially column 8 at lines 25-49). US Patent No. 4,772,547 further discloses enhancing immunogenicity of the peptides by coupling the peptides covalently (via Cys, i.e., by "crosslinking") to toxoids or carrier materials that enhance immunogenicity. Claim 26 is included in the instant rejection because the instant specification discloses conjugation being in the nature of a chemical or molecular crosslink (page 15 at lines 25-30).

US Patent No. 4,772,547 does not disclose a heteroconjugate comprising anti-CD3 mAb directed against the non-polymorphic TCR-associated CD3 chains, γ, δ, ε or ζ coupled or fused to a second protein having an epitope against which a cellular or humoral immune response is desired.

Mezzanzanica et al teach anti-CD3 mAb OKT3 and a defined target antigen on human ovarian carcinoma cells and an antibody against the said antigen (especially page 609, column 2, MAbs section). Mezzanzanica et al further teach antibodies comprising anti-CD3 antibodies administered in humans to induce T cells.

Anderson et al teach the activation of T cells and NK cells using anti-CD3 mAb and IL-2 for anti-tumor activity. Anderson et al further teach the anti-human CD3 mAb, OKT3.

EP 0273716 A2 teaches HIV gp120 envelope protein antigen of HIV and T1 and T2 antigenic peptides and treatment of HIV (especially page 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the mAb OKT3 taught by Mezzanzanica et al and Anderson et al in the composition disclosed by US Patent No. 4,772,547 comprising antigenic peptides from viral proteins such as HIV or those HIV antigenic peptides taught by EP 0273716 A2 or comprising tumor antigens such as those taught by Mezzanzanica et al and adjuvants such as IL-2 disclosed by US Patent No. 4,772,547 or as taught by Anderson et al, and in addition, to have cross-linked the OKT3 mAb to the said antigenic peptide(s).

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a composition that could stimulate T cells for anti-tumor or anti-viral immunity because US Patent No. 4,772,547 discloses coupling peptides covalently by cross-linkage to a carrier material to enhance immunogenicity and use with IL-2 in anti-viral vaccine compositions, Anderson et al teach the activation of T cells using anti-CD3 mAb such as OKT3 for activation of anti-tumor T cell immunity, since Mezzanzanica et al teach antibodies comprising anti-CD3 antibodies administered in humans to induce T cells, and since Mezzanzanica et al teach target tumor antigens, US Patent No. 4,772,547 discloses viral peptide antigens for vaccine use, and EP 0273716 A2 teaches the HIV T1 and T2 antigenic peptides and treatment of HIV.

The motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Section MPEP 2144.07.

9. Claims 1, 8, 16-19, 21-24, 26 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 4,772,547 (previously provided) in view of Ellenhorn et al (Science, 242(4878): 569-571, 10/28/88, IDS reference "C39"), Mezzanzanica et al (Int. J. Cancer, 41, 609-615, 1988, previously provided) and EP 0273716A2 (previously provided).

US Patent No. 4,772,547 discloses vaccine compositions comprising antigenic peptides and proteins from hepatitis surface antigens and HIV envelope and adjuvants such as IFN, IL-2, thymosin alpha 1 (especially column 8 at lines 25-49). US Patent No. 4,772,547 further discloses enhancing immunogenicity of the peptides by coupling the peptides covalently (via Cys, i.e., by "crosslinking") to toxoids or carrier materials that enhance immunogenicity. Claim 26 is included in the instant rejection because the instant specification discloses conjugation being in the nature of a chemical or molecular crosslink (page 15 at lines 25-30).

US Patent No. 4,772,547 does not disclose a heteroconjugate comprising anti-CD3 mAb directed against the non-polymorphic TCR-associated CD3 chains, γ, δ, ε or ζ coupled or fused to a second protein having an epitope against which a cellular or humoral immune response is desired.

Ellenhorn et al teach in vivo administration of anti-CD3, including the mAb 145-C11, for treatment of tumors.

Mezzanzanica et al teach anti-CD3 mAb OKT3 and a defined target antigen on human ovarian carcinoma cells and an antibody against the said antigen (especially page 609, column 2, MAbs section). Mezzanzanica et al further teach antibodies comprising anti-CD3 antibodies administered in humans to induce T cells.

EP 0273716 A2 teaches HIV gp120 envelope protein antigen of HIV and T1 and T2 antigenic peptides and treatment of HIV (especially page 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the mAb OKT3 taught by Mezzanzanica et al or that taught by Ellenhorn et al in the composition disclosed by US Patent No. 4,772,547 comprising antigenic peptides from viral proteins such as HIV or those HIV antigenic peptides taught by EP 0273716 A2 or comprising tumor antigens such as those taught by Mezzanzanica et al and adjuvants such as IL-2 disclosed by US Patent No. 4,772,547 or as taught by Anderson et al, and in addition, to have cross-linked the anti-CD3 mAb to the said antigenic peptide(s).

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a composition that could stimulate T cells for anti-tumor or anti-viral immunity because US Patent No. 4,772,547 discloses coupling peptides covalently by cross-linkage to a carrier material to enhance immunogenicity and use with IL-2 in anti-viral vaccine compositions, Ellenhorn et al teach the activation of T cells using anti-CD3 mAb for activation of anti-tumor T cell immunity in vivo, since Mezzanzanica et al teach anti-CD3 antibodies administered in humans to induce T cells, and since Mezzanzanica et al teach target tumor antigens, US Patent No. 4,772,547 discloses viral peptide antigens for vaccine use, and EP 0273716 A2 teaches the HIV T1 and T2 antigenic peptides and treatment of HIV.

The motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Section MPEP 2144.07.

10. It appears that there is a typographical error in withdrawn claim 14, i.e., the deletion of "a" before "bispecific" at line 2.

11. The Declaration of Jeffrey A. Bluestone under 37 CFR 1.132 filed 3/12/04 has overcome the 102 rejections of record in the previous Office Action.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end

of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Wednesday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Chan Y Christina, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600
July 14, 2004

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600